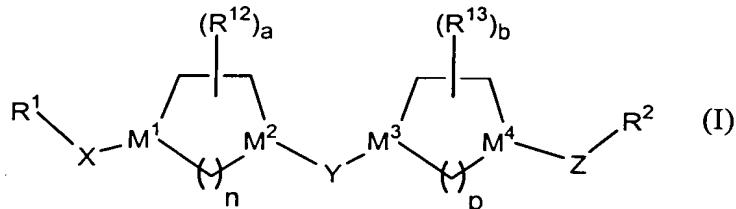


**WHAT IS CLAIMED IS:**

1. A compound of the formula:



or a pharmaceutically acceptable salt or solvate thereof, wherein:

(1)  $R^1$  is selected from:

- (a) aryl;
- (b) heteroaryl;
- (c) heterocycloalkyl
- (d) alkyl;
- (e) cycloalkyl; or
- (f) alkylaryl;

wherein said  $R^1$  groups are optionally substituted with 1 to 4 substituents

10 independently selected from:

- (1) halogen;
- (2) hydroxyl;
- (3) lower alkoxy;
- (4)  $-CF_3$ ;
- (5)  $CF_3O-$ ;
- (6)  $-NR^4R^5$ ;
- (7) phenyl;
- (8)  $-NO_2$ ;
- (9)  $-CO_2R^4$ ;
- (10)  $-CON(R^4)_2$  wherein each  $R^4$  is the same or different;
- (11)  $-S(O)_mN(R^{20})_2$  wherein each  $R^{20}$  is the same or different H or alkyl group, preferably  $C_1$  to  $C_4$  alkyl, most preferably  $C_1$ - $C_2$  alkyl, and more preferably methyl;
- (12)  $-CN$ ; or

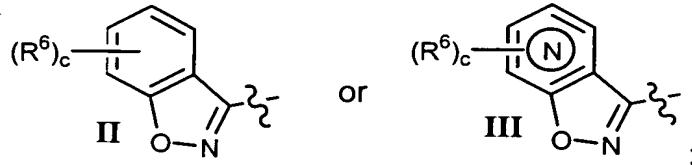
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25

(13) alkyl; or

(2)  $R^1$  and  $X$  taken together form a group selected from:



(3)  $X$  is selected from:  $=\text{C}(\text{O})$ ,  $=\text{C}(\text{NOR}^3)$ ,  $=\text{C}(\text{NNR}^4\text{R}^5)$ ,



(4)  $M^1$  is carbon;

(5)  $M^2$  is selected from C or N;

(6)  $M^3$  and  $M^4$  are independently selected from C or N;

(7)  $Y$  is selected from: is  $-\text{CH}_2-$ ,  $=\text{C}(\text{O})$ ,  $=\text{C}(\text{NOR}^{20})$  (wherein  $\text{R}^{20}$  is as

10 defined above), or  $=\text{C}(\text{S})$ ;

(8)  $Z$  is a  $\text{C}_1 - \text{C}_6$  alkyl group;

(9)  $R^2$  is a five or six-membered heteroaryl ring, said six-membered heteroaryl ring comprising 1 or 2 nitrogen atoms with the remaining ring atoms being carbon, and said five-membered heteroaryl ring containing 1 or 2 heteroatoms

15 selected from: nitrogen, oxygen, or sulfur with the remaining ring atoms being carbon; said five or six membered heteroaryl rings being optionally substituted with 1 to 3 substituents independently selected from: halogen, hydroxyl, lower alkyl, lower alkoxy,  $-\text{CF}_3$ ,  $\text{CF}_3\text{O}-$ ,  $-\text{NR}^4\text{R}^5$ , phenyl,  $-\text{NO}_2$ ,  $-\text{CO}_2\text{R}^4$ ,  $-\text{CON}(\text{R}^4)_2$  wherein each  $\text{R}^4$  is the same or different,  $-\text{CH}_2\text{NR}^4\text{R}^5$ ,  $-(\text{N})\text{C}(\text{NR}^4\text{R}^5)_2$ , or  $-\text{CN}$ ;

20 (10)  $R^3$  is selected from:

(a) hydrogen;

(b)  $\text{C}_1 - \text{C}_6$  alkyl;

(c) aryl;

(d) heteroaryl;

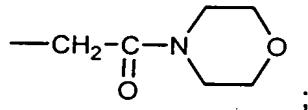
25 (e) heterocycloalkyl;

(f) arylalkyl;

(g)  $-(\text{CH}_2)_e-\text{C}(\text{O})\text{N}(\text{R}^4)_2$  wherein each  $\text{R}^4$  is the same or different,

(h)  $-(\text{CH}_2)_e-\text{C}(\text{O})\text{OR}^4$ ;

(i)  $-(CH_2)_e-C(O)R^{30}$  wherein  $R^{30}$  is a heterocycloalkyl group, such as, for example, morpholinyl, piperidinyl, piperazinyl or pyrrolidinyl, including



(j)  $-CF_3$ ; or

5 (k)  $-CH_2CF_3$ ;

wherein said aryl, heteroaryl, heterocycloalkyl, and the aryl portion of said arylalkyl are optionally substituted with 1 to 3 substituents selected from: halogen,  $-OH$ ,  $-OCF_3$ ,  $-CF_3$ ,  $-CN$ ,  $-N(R^{45})_2$ ,  $-CO_2R^{45}$ , or  $-C(O)N(R^{45})_2$ , wherein each  $R^{45}$  is independently selected from: H, alkyl, alkylaryl, or alkylaryl wherein said aryl moiety is substituted

10 with 1 to 3 substituents independently selected from  $-CF_3$ ,  $-OH$ , halogen, alkyl,  $-NO_2$ , or  $-CN$ ;

(11)  $R^4$  is selected from: hydrogen,  $C_1 - C_6$  alkyl, aryl, alkylaryl, said aryl and alkylaryl groups being optionally substituted with 1 to 3 substituents selected from: halogen,  $-CF_3$ ,  $-OCF_3$ ,  $-OH$ ,  $-N(R^{45})_2$ ,  $-CO_2R^{45}$ ,  $-C(O)N(R^{45})_2$ , or  $-CN$ ; wherein  $R^{45}$  is as defined above;

(12)  $R^5$  is selected from: hydrogen,  $C_1 - C_6$  alkyl,  $-C(O)R^4$ ,  $-C(O)_2R^4$ , or  $-C(O)N(R^4)_2$  wherein each  $R^4$  is independently selected, and  $R^4$  is as defined above;

(13) or  $R^4$  and  $R^5$  taken together with the nitrogen atom to which they are bound forms a five or six membered heterocycloalkyl ring;

20 (14)  $R^6$  is selected from: alkyl, aryl, alkylaryl, halogen, hydroxyl, lower alkoxy,  $-CF_3$ ,  $CF_3O-$ ,  $-NR^4R^5$ , phenyl,  $-NO_2$ ,  $-CO_2R^4$ ,  $-CON(R^4)_2$  wherein each  $R^4$  is the same or different, or  $-CN$ ;

(15)  $R^{12}$  is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(16)  $R^{13}$  is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

25 (17) a is 0 to 2;

(18) b is 0 to 2;

(19) c is 0 to 2;

(20) e is 0 to 5;

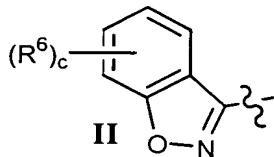
(21) m is 1 or 2;

30 (22) n is 1, 2 or 3; and

(23)  $p$  is 1, 2 or 3, with the proviso that when  $M^3$  and  $M^4$  are both nitrogen, then  $p$  is 2 or 3.

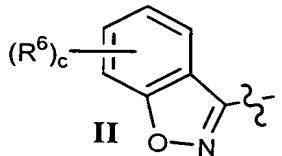
2. The compound of Claim 1 wherein  $R^1$  is selected from:

5 (A) aryl;  
(B) substituted aryl, wherein the substituents on said substituted aryl are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;  
(C) heteroaryl;  
(D) substituted heteroaryl; or  
10 (E) when  $R^1$  is taken together with  $X$ , then the moiety is



3. The compound of Claim 2 wherein  $R^1$  is selected from:

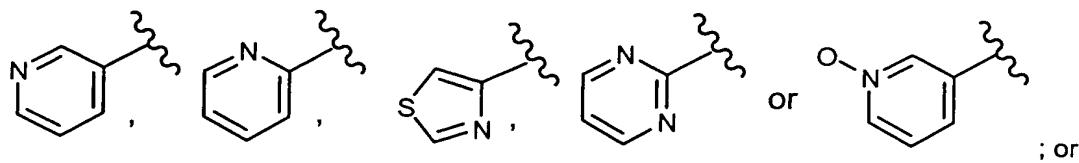
15 (A) phenyl;  
(B) substituted phenyl wherein the substituents on said substituted phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;  
(C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide;  
(D) alkyl substituted thiazolyl; or  
20 (E) when  $R^1$  is taken together with  $X$ , then the moiety is



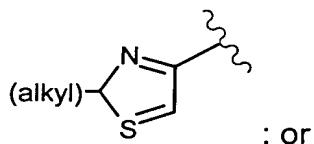
wherein  $c$  is 0 or 1, and when  $c$  is 1 then  $R^6$  is halo.

4. The compound of Claim 3 wherein  $R^1$  is selected from:

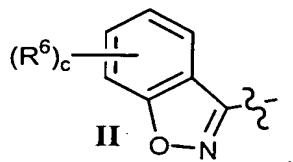
25 (A) phenyl;  
(B) substituted phenyl, wherein the substituents on said substituted phenyl are independently selected from: chloro, fluoro or trifluoromethyl;  
(C) heteroaryl selected from:



(D) substituted heteroaryl of the formula:



(E) when  $R^1$  is taken together with X, then the moiety is



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wherein c is 0 or 1, and when c is 1 then  $R^6$  is fluoro.

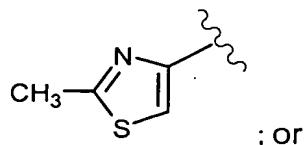
5. The compound of Claim 1 wherein  $R^1$  is selected from:

(A) phenyl;

10 (B) substituted phenyl, wherein the substituents on said substituted phenyl are independently selected from: chloro, fluoro or trifluoromethyl;

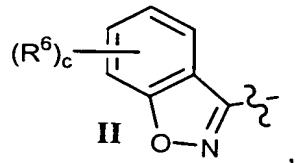
(C) pyridyl; or

(D) substituted heteroaryl of the formula:



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(E) when  $R^1$  is taken together with X, then the moiety is

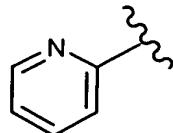


wherein c is 0 or 1, and when c is 1 then  $R^6$  is fluoro.

6. The compound of Claim 5 wherein  $R^1$  is pyridyl.

20

7. The compound of Claim 6 wherein R<sup>1</sup> is



8. The compound of Claim 1 wherein X is =C(NOR<sup>3</sup>), and R<sup>3</sup> is selected  
5 from H or alkyl.

9. The compound of Claim 8 wherein R<sup>3</sup> is selected from H, methyl or  
10 ethyl.

10. The compound of Claim 9 wherein R<sup>3</sup> is methyl.

11. The compound of claim 1 wherein: (1) M<sup>2</sup> is nitrogen; and (2) M<sup>3</sup> and M<sup>4</sup>  
are selected such that: (a) one is carbon and the other is nitrogen, or (b) both are  
nitrogen.

15

12. The compound of Claim 11 wherein M<sup>3</sup> is carbon, and M<sup>4</sup> is nitrogen.

13. The compound of Claim 1 wherein:

n is 2;.

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a is 0 or 1;

b is 0 or 1;

c is 0 or 1, and when c is 1 then R<sup>6</sup> is halo;

e is 1 to 5; and

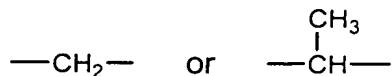
p is 2.

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14. The compound of claim 1 wherein Y is =C(O).

15. The compound of Claim 1 wherein Z is C<sub>1</sub> to C<sub>3</sub> alkyl.

16. The compound of Claim 1 wherein Z is



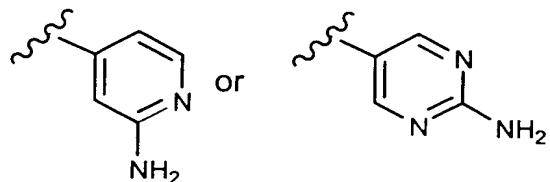
17. The compound of Claim 1 wherein R<sup>2</sup> is a six membered heteroaryl ring.

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18. The compound of Claim 17 wherein R<sup>2</sup> is selected from pyridyl, pyridyl substituted with —NR<sup>4</sup>R<sup>5</sup>, pyrimidinyl, or pyrimidinyl substituted with —NR<sup>4</sup>R<sup>5</sup>.

10 19. The compound of Claim 18 wherein R<sup>2</sup> is pyridyl substituted with —NH<sub>2</sub>, or pyrimidinyl substituted with —NH<sub>2</sub>.

20. The compound of Claim 19 wherein R<sup>2</sup> is



15 21. The compound of Claim 1 wherein R<sup>4</sup> is H or lower alkyl; R<sup>5</sup> is H, C<sub>1</sub> to C<sub>6</sub>alkyl, or —C(O)R<sup>4</sup>; R<sup>12</sup> is alkyl, hydroxy or fluoro; and R<sup>13</sup> is alkyl, hydroxy or fluoro.

22. The compound of Claim 21 wherein R<sup>4</sup> is H or methyl; R<sup>5</sup> is H or methyl; R<sup>12</sup> is hydroxy or fluoro; and R<sup>13</sup> is hydroxy or fluoro.

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23. The compound of Claim 1 wherein:

(1) R<sup>1</sup> is selected from:

(A) aryl;

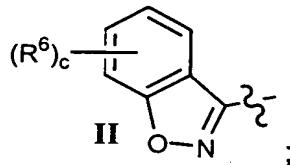
(B) substituted aryl, wherein the substituents on said substituted aryl

25 are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;

(C) heteroaryl; or

(D) substituted heteroaryl; or

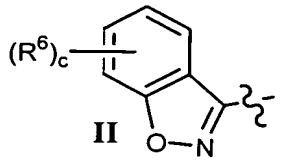
(E) when R<sup>1</sup> is taken together with X, then the moiety is



(2) X is =C(NOR<sup>3</sup>);  
(3) R<sup>3</sup> is selected from H or alkyl;  
5 (4) M<sup>2</sup> is nitrogen;  
(5) Y is =C(O);  
(6) M<sup>3</sup> and M<sup>4</sup> are selected such that: (1) one is carbon and the other is nitrogen, or (2) both are nitrogen;  
(7) Z is C<sub>1</sub> to C<sub>3</sub> alkyl; and  
10 (8) R<sup>2</sup> is a six membered heteroaryl ring.

24. The compound of Claim 23 wherein:

(1) R<sup>1</sup> is selected from:  
(A) phenyl;  
15 (B) substituted phenyl wherein the substituents on said substituted phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;  
(C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide; or  
(D) alkyl substituted thiazolyl; or  
20 (E) when R<sup>1</sup> is taken together with X, then the moiety is

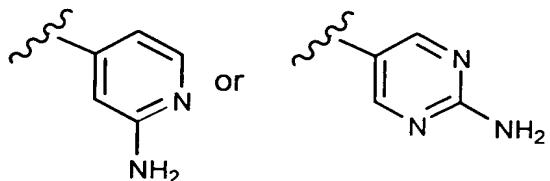


wherein c is 0 or 1, and when c is 1 then R<sup>6</sup> is halo;

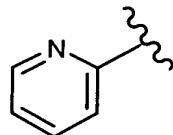
(2) R<sup>3</sup> is selected from H, methyl or ethyl;  
(3) n is 2,  
25 (4) a is 0 or 1,  
(5) b is 0 or 1,  
(6) c is 0 or 1 and when c is 1 then R<sup>6</sup> is halo,  
(7) e is 1 to 5,

(8)  $p$  is 2,  
(9)  $R^4$  is H or lower alkyl,  
(10)  $R^5$  is H,  $C_1$  to  $C_6$ alkyl, or  $-C(O)R^4$ ;  
(11)  $R^{12}$  is alkyl, hydroxy or fluoro, and  
5 (12)  $R^{13}$  is alkyl, hydroxy or fluoro.

25. The compound of Claim 24 wherein  $R^2$  is



10  $R^1$  is



$M^2$  is nitrogen,  $M^3$  is carbon, and  $M^4$  is nitrogen.

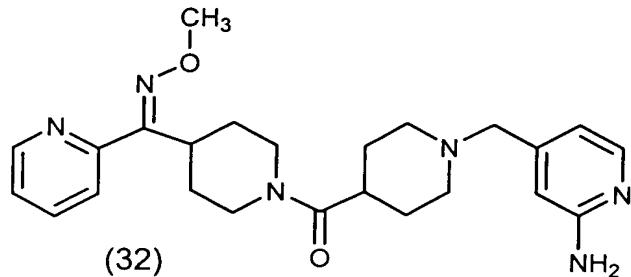
15 26. The compound of Claim 1 selected from: Compound 23, 30, 31, 32, 33, 41, 44, 45, 49, 50, 52, 53, 54, 55, 56, 57A, 59, 65, 75, 76, 80, 82, 83, 88, 92, 99, 104, 105, 110, 111, 117, 121, 123, 127, 128, 200-241, 244-273, 275, 278-282, 287, 296, 301-439, or 446.

20 27. The compound of Claim 1 selected from: Compound 23, 30, 31, 32, 33, 50, 53, 54, 55, 56, 57A, 59, 92, 212, 215, 218, 219, 220, 224, 225, 226, 227, 229, 233, 235, 237, 238, 246, 246A, 247, 248, 251, 253, 253A, 268-273, 275, 278-281, 287, 296, 301, 304-307, 309, 312, 314-318, 320-356, or 358-376.

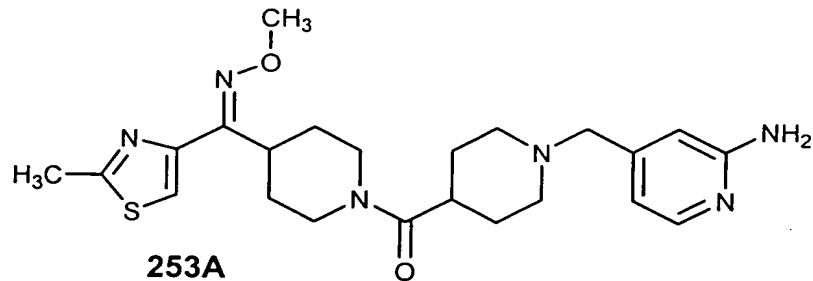
25 28. The compound of Claim 1 selected from: Compound 30, 31, 32, 33, 54, 55, 56, 57A, 225, 237, 246A, 253A, 273, or 280, 287, 296, 301, 304-307, 309, 312, 314-318, 320-348, 350-356, 359-372, or 374-376.

29. The compound of Claim 1 selected from: Compound 32, 54, 55, 253A, 287 or 320.

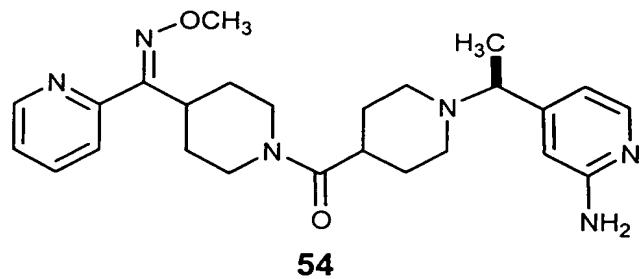
30. The compound of Claim 1 having the formula:



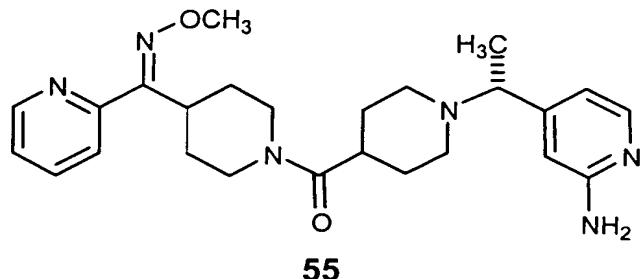
31. The compound of Claim 1 having the formula:



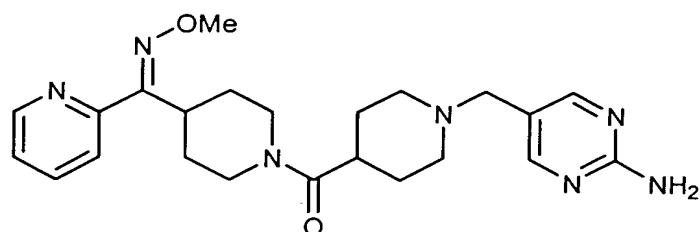
10 32. The compound of Claim 1 having the formula:



33. The compound of Claim 1 having the formula:



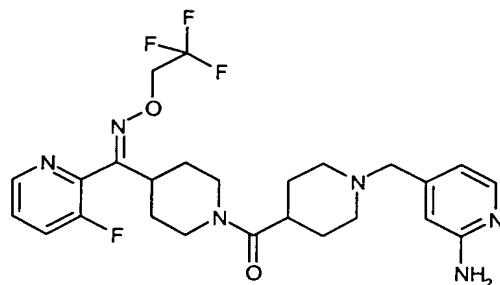
34. The compound of Claim 1 having the formula:



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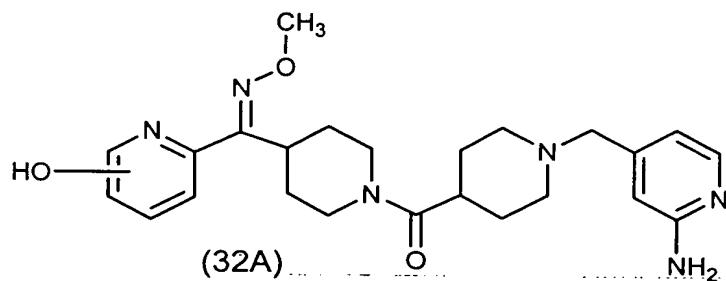
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35. The compound of Claim 1 having the formula:

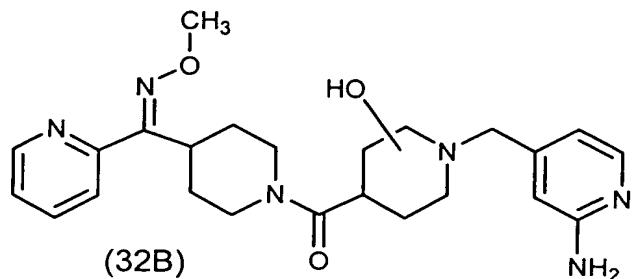


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36. The compound of Claim 1 having the formula:



37. The compound of Claim 1 having the formula:



38. A pharmaceutical composition comprising an effective amount of a  
5 compound of Claim 1 and a pharmaceutically effective carrier.

39. A method of treating: allergy, allergy-induced airway responses,  
congestion, cardiovascular disease, diseases of the GI tract, hyper and hypo motility  
and acidic secretion of the gastro-intestinal tract, obesity, sleeping disorders,  
10 disturbances of the central nervous system, attention deficit hyperactivity disorder,  
hypo and hyperactivity of the central nervous system, Alzheimer's disease,  
schizophrenia, and migraine comprising administering to a patient in need of such  
treatment an effective amount of a compound of Claim 1.

15 40. The method of Claim 39 wherein allergy-induced airway responses are  
treated.

41. The method of Claim 39 wherein allergy or nasal congestion is treated.

20 42. A pharmaceutical composition comprising an effective amount of a  
compound of Claim 1, and an effective amount of H<sub>1</sub> receptor antagonist, and a  
pharmaceutically effective carrier.

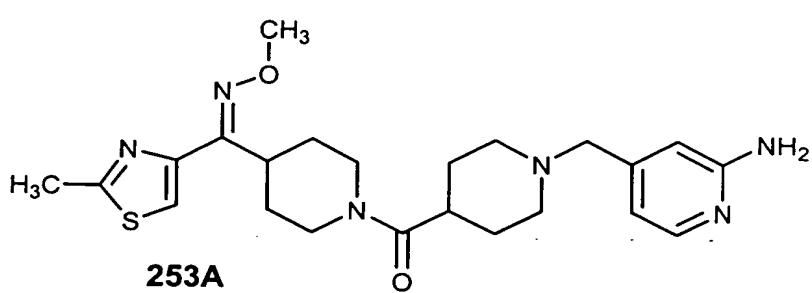
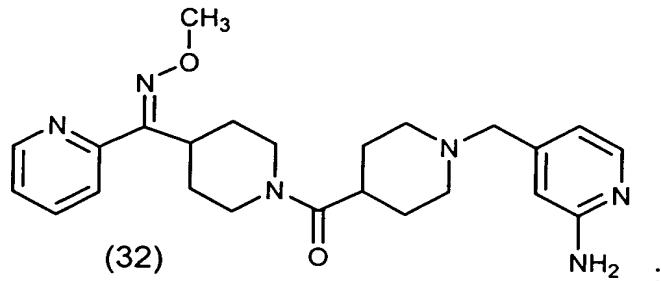
25 43. A method of treating: allergy, allergy-induced airway responses, and  
congestion comprising administering to a patient in need of such treatment an  
effective amount of a compound of Claim 1 in combination with an effective amount of  
an H<sub>1</sub> receptor antagonist.

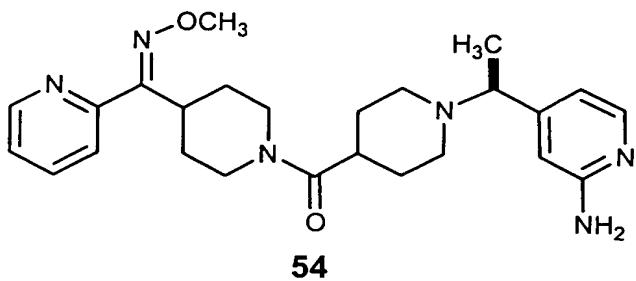
44. The method of Claim 43 wherein said H<sub>1</sub> receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine, chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, 5 epinastine, eflterizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, pyrilamine, promethazine, terfenadine, tripeleannamine, temelastine, trimeprazine or triprolidine.

10 45. The method of Claim 44 wherein said H<sub>1</sub> receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

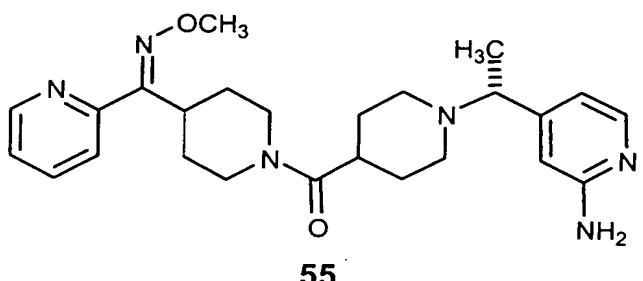
15 46. The method of Claim 45 wherein said H<sub>1</sub> receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

47. A pharmaceutical composition comprising an effective amount of a compound of Claim 1 and a pharmaceutically effective carrier, wherein said compound of Claim 1 is selected from:



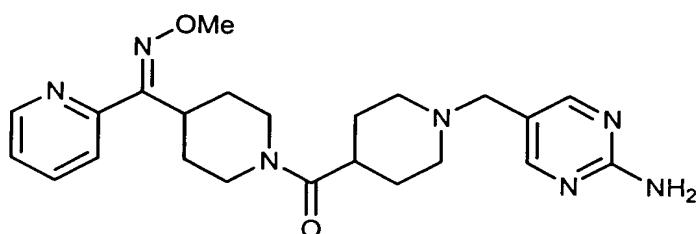


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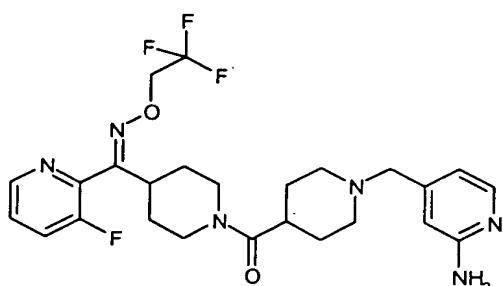
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; or

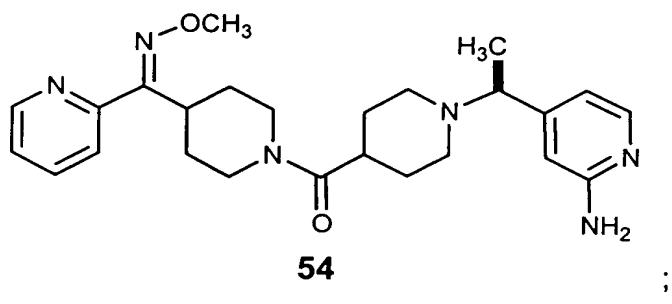
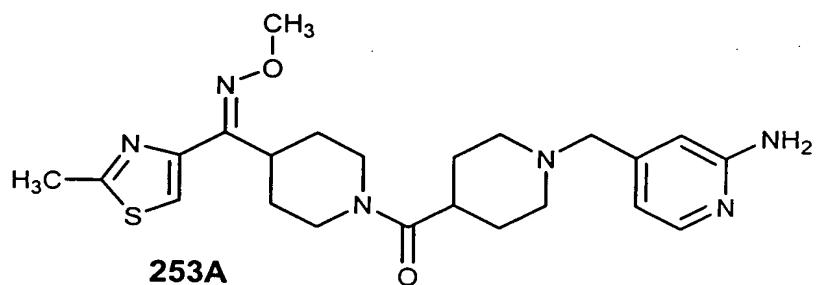
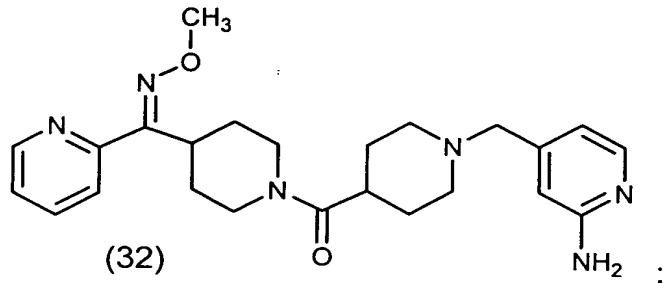


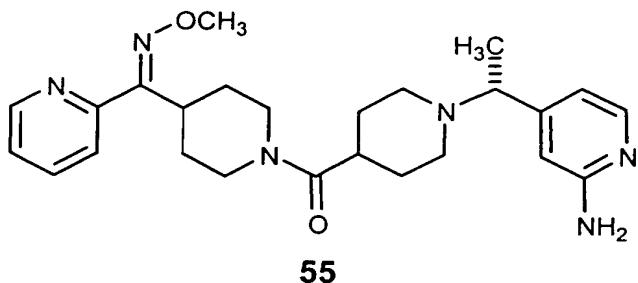
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48. A method of treating: allergy, allergy-induced airway responses, congestion, cardiovascular disease, diseases of the GI tract, hyper and hypo motility

and acidic secretion of the gastro-intestinal tract, obesity, sleeping disorders, disturbances of the central nervous system, attention deficit hyperactivity disorder, hypo and hyperactivity of the central nervous system, Alzheimer's disease, schizophrenia, and migraine comprising administering to a patient in need of such

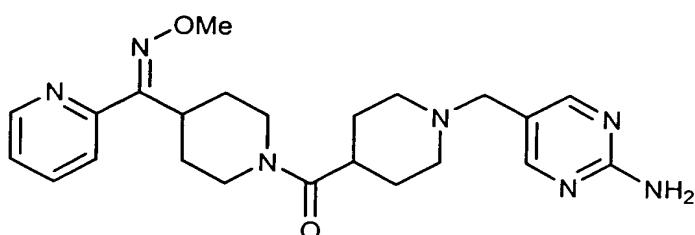
5 treatment an effective amount of a compound of Claim 1, wherein said compound of Claim 1 is selected from:





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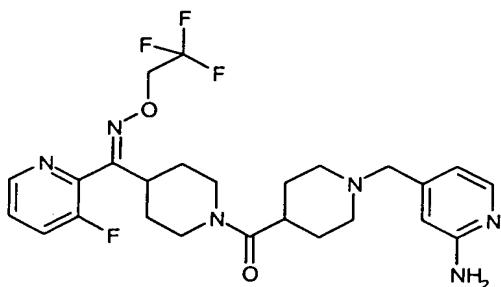
;



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; or

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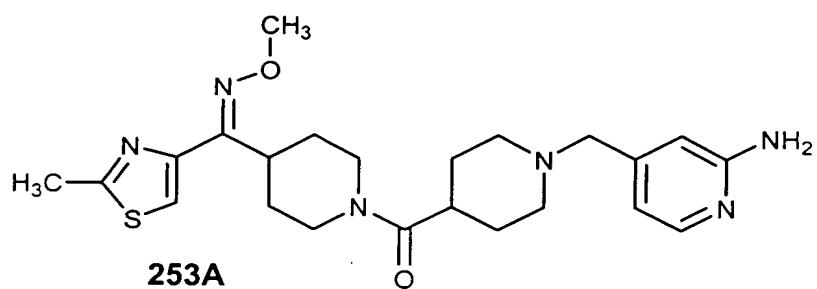
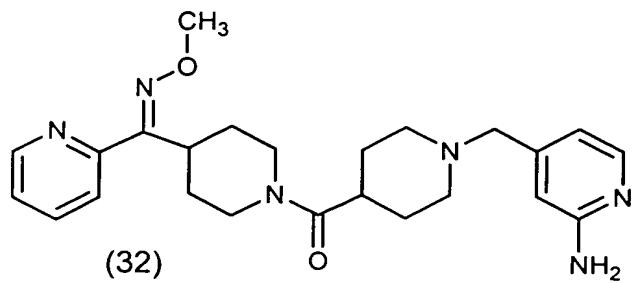
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49. The method of Claim 48 wherein allergy-induced airway responses are treated.

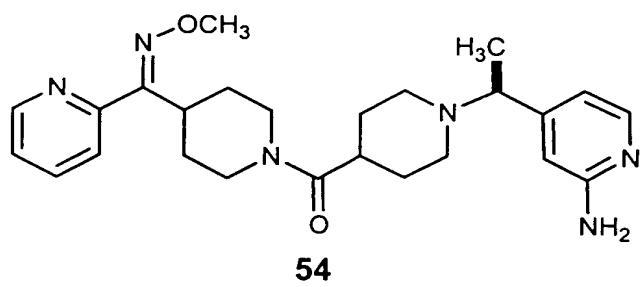
50. The method of Claim 48 wherein allergy or nasal congestion is treated.

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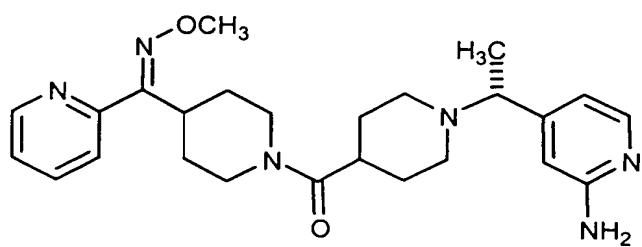
51. A pharmaceutical composition comprising an effective amount of a compound of Claim 1, and an effective amount of H<sub>1</sub> receptor antagonist, and a pharmaceutically effective carrier, wherein said compound of Claim 1 is selected from:

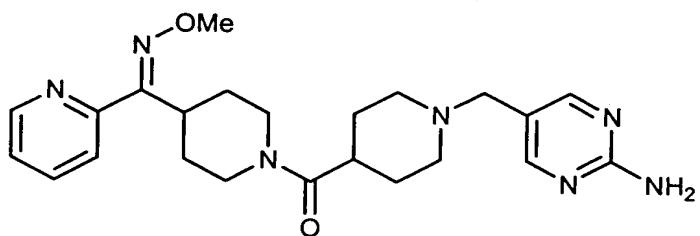


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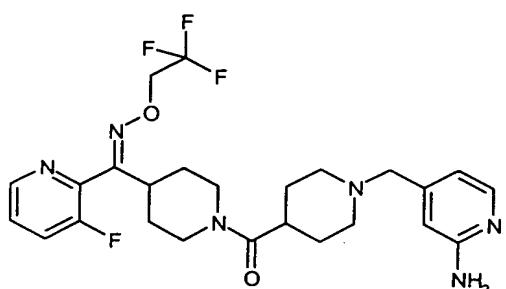
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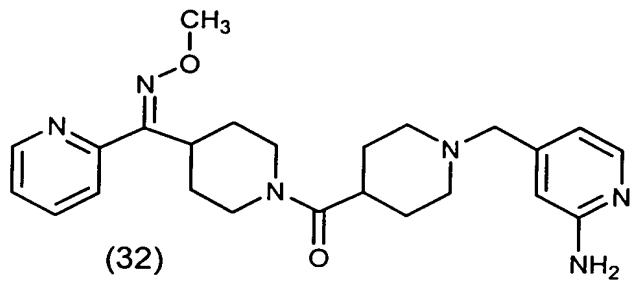
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; or

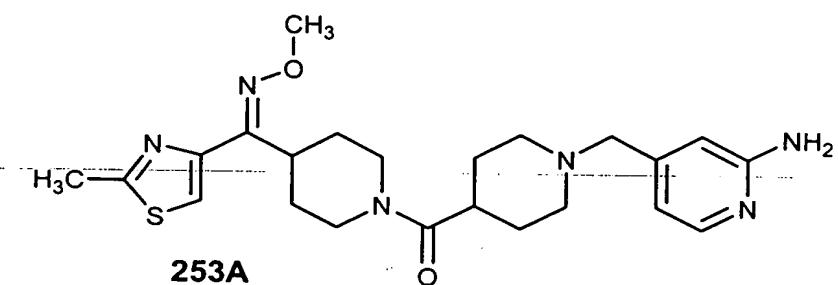


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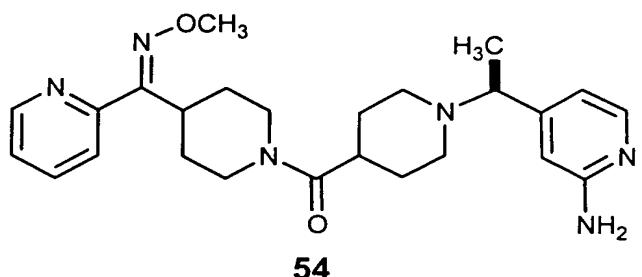
52. A method of treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of Claim 1 in combination with an effective amount of an H<sub>1</sub> receptor antagonist, wherein said compound of Claim 1 is selected from:



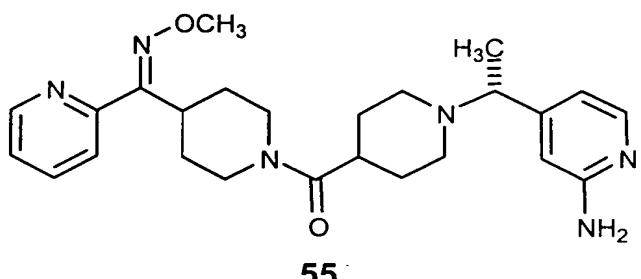
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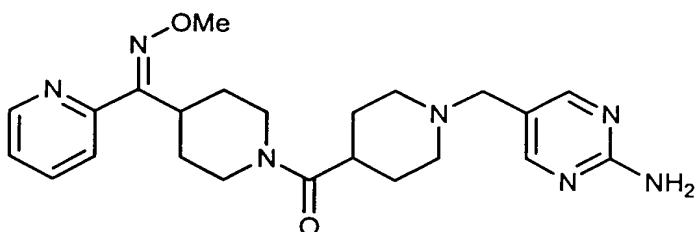


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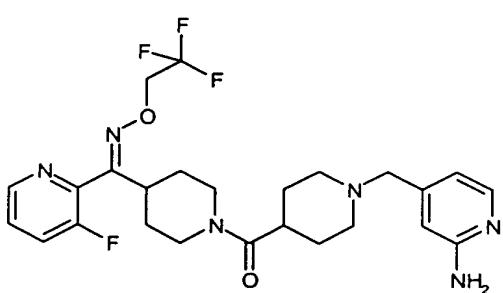
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; or

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53. The method of Claim 52 wherein said H<sub>1</sub> receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine,

chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, epinastine, efletirizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, 5 pyrilamine, promethazine, terfenadine, tripeleannamine, temelastine, trimeprazine or triprolidine.

54. The method of Claim 53 wherein said H<sub>1</sub> receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

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55. The method of Claim 54 wherein said H<sub>1</sub> receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

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